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### **AMENDMENTS TO THE DRAWINGS**

Applicants have corrected the typographical error in Figures 3A and 3C by replacing the number 154 with 302, thereby identifying “channel layer 302.” Applicants have also identified “channel layer 302” in Figure 3B. Substitute sheets for 3A-3C are submitted herewith.

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### **REMARKS**

Claims 1, 5-9 and 11-20 are pending. Claims 2-4 and 10 have been cancelled. Claims 11-20 have been added. Claims 1, 5 and 7 have been amended to clarify and/or broaden the claimed subject matter. These amendments are fully supported by the specification as originally filed, for example, page 2, lines 6-18; page 6, lines 1-8; and page 35, lines 8 through 9. Support for new Claims 11-20 can be found on page 36, lines 4 through 20; page 35, lines 8 through 9; and elsewhere throughout the specification.

Applicants have also amended Figures 3A-3C so as to indicate "channel layer 302." None of the foregoing amendments to the drawings or the specification add new matter to the instant application.

After having carefully considered the Office Action mailed on August 6, 2004, Applicants respectfully traverse the all of the Examiner's claim rejections and objections.

### **Drawings**

The Examiner objects to Figures 3A-3C as failing to comply with 37 C.F.R. § 1.84(p)(5). Specifically, the Examiner maintains that "channel layer 302" mentioned in the description is not in Figures 3A-3C.

Applicants have corrected Figures 3A and 3C by replacing the number 154 with 302. Additionally, Applicants have identified "channel layer 302" in Figure 3B. The substitute drawing sheets provided herewith reflect these corrections. As such, Applicants respectfully request that the Examiner reconsider and withdraw the objection to the drawings.

### **Rejection Under 35 U.S.C. § 112, second paragraph – Indefiniteness**

The Examiner rejects Claims 1-10 as failing to particularly point out and distinctly claim the invention. Regarding Claim 1, the Examiner asserts that the phrase "for use" is vague and indefinite since the specification allegedly does not define "use" or make it clear how the "solid phase" is to be used in a "dual bead assay". The Examiner also alleges that the phrase "presence or absence of a cross-linking agent" is vague and indefinite. According to the Examiner, it is not clear whether the method as claimed would include or not include the cross-linking agent. The Examiner also alleges that the phrases "determining the percentage of probe bound covalently to the solid phase" and "calculating the percentage of probe bound covalently to the solid phase"

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recite the same limitation, and thereby render Claim 1 unclear and confusing. Finally, the Examiner asserts that Claim 1 is indefinite because it contains the term "approximately", and the specification allegedly does not provide a standard for ascertaining the requisite degree.

Applicants maintain that Claim 1, as well as the claims dependent thereon, are clear and definite. Regarding the rejection of Claim 1 based on the phrase "for use", Applicants maintain that the specification, including the drawings, provide several non-limiting examples of the use of solid phases in the dual bead assays. Nevertheless, in the interest of advancing the prosecution of the instant application, Claim 1 has been amended to delete the phrase "for use." To further expedite prosecution, Claim 1 has also been amended to delete the allegedly unclear phrase "presence or absence of a cross-linking agent" and to replace the first occurrence of the term "percent" with the term "amount."

Regarding the rejection of Claim 1 based on the use of the term "approximately", Applicants maintain that, in view of the specification, one of ordinary skill in the art would recognize that, in some cases, a calculated percent covalent binding value which is less than 80%, but which is substantially close to 80%, would indicate that the test solid surface is suitable for its intended purpose. In an exemplary case, the percentage of covalent binding may be calculated at 79.5%. Although 79.5% is not exactly 80%, it is approximately 80%. A skilled artisan would recognize this and other examples as values that are approximately 80%. It is well established that terms allowing some degree of flexibility, such as the terms "substantially," "about" and "essentially" can be properly used without violating 35 U.S.C. §112, paragraph 2. See MPEP §2173.05(b). The term "approximately" does not raise any different issues than the well-accepted term "substantially." As such, the use of the term "approximately" in claim 1 is clear and definite.

In view of the foregoing remarks, Applicants respectfully request that the Examiner reconsider and withdraw the rejections of Claim 1, as well as claims dependent thereon, under 35 U.S.C. § 112, second paragraph.

#### **Rejection Under 35 U.S.C. § 102(b)**

The Examiner rejects Claims 1-2, and 5-8 under 35 U.S.C. § 102(b) as being anticipated by Sutton et al. (U.S. Patent No. 5,147,777, hereinafter Sutton). According to the Examiner, Sutton discloses preparing polymeric particles with covalently attached radiolabeled protein by

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using two different activating agents. In particular, the Examiner alleges that Sutton teaches the calculation of the percentage of radiolabeled protein covalently bound to the polymeric particles. The Examiner further asserts that Sutton discloses that 90% of the radiolabeled protein covalently bound to the particles, such that the “reagents prepared acceptably bind antibody for use in immunoassays.” The Examiner also asserts that Sutton discloses each of the additional limitations present in Claims 2 and 5-8.

Applicants respectfully disagree that this rejection should be applied to the current claims. To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). “Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference. ...There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention.” *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991).

Sutton does not anticipate Claims 1-2 and 5-8 because it fails to teach all the elements and limitations of those claims. Claim 1 is drawn to a method of evaluating suitability of a solid phase as a biodisc surface. As amended, this claim recites the steps of obtaining a biodisc, wherein at least one surface of the biodisc comprises a test solid phase, binding a probe or capture agent to the test solid phase, determining the amount of probe or capture agent covalently bound and non-covalently to the test solid phase and calculating the percentage of probe bound covalently to the test solid phase. Sutton does not disclose obtaining a biodisc, wherein at least one surface of the biodisc comprises a test solid phase. As such, Sutton does not anticipate Claim 1 or any of the claims dependent thereon.

In view of the foregoing, Applicants respectfully request that the Examiner withdraw the rejection of Claims 1, 2 and 5-8 as anticipated under 35 U.S.C. § 102(b).

Sutton does not anticipate new claims 11-20. Independent claim 11 is drawn to a method of evaluating the suitability of a solid phase as a binding surface in a biodisc. This method recites the steps of selecting a test solid phase, binding a probe or capture agent to a first and a second sample of the test solid phase, in a first and a second binding reaction, respectively, wherein said first binding reaction comprises a cross-linking agent and said second binding reaction lacks a cross-linking agent, determining the total amount of probe or capture agent bound to the first

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sample of the test solid phase and to the second sample of the test solid phase, and comparing the total amount of probe or capture agent bound to the first sample of the test solid phase to the total amount of probe or capture agent bound to the second sample of the test solid phase. Sutton does not teach treating the solid phase or polymeric particles with probe in the absence of a cross-linking agent. Rather, Sutton discloses only performing a single binding reaction in the presence of a cross-linking agent. As such, Sutton fails to disclose every element of any of the newly added claims.

In view of the foregoing remarks, Applicants respectfully request that the Examiner reconsider and withdraw all rejections under 35 U.S.C. § 102(b).

**Rejection Under 35 U.S.C. § 103(a)**

The Examiner rejects Claim 3 under 35 U.S.C. § 103(a) as being unpatentable over Sutton in view of Ullman et al. (US Patent No. 6,103,537, hereinafter Ullman). Specifically, the Examiner asserts that Sutton teaches latex particles which facilitate attachment of proteins or other biological compounds, but does not disclose magnetic beads. According to the Examiner, Ullman teaches magnetic beads preactivated to covalently bind protein, such that the covalently modified magnetic beads are capable of capturing receptors of interest, and further that detection of the receptors is facilitated through immobilization of the magnetic beads by application of a magnetic field. The Examiner asserts that it would have been obvious to modify the method of Sutton with the magnetic latex beads taught by Ullman to capture receptors of interest. The Examiner alleges that one of skill in the art would have a reasonable expectation for success, since the particles taught by Sutton and the beads taught by Ullman both covalently bind proteins. The Examiner also alleges that colored latex beads and magnetic latex beads are well known in the art as being functionally equivalent.

The Examiner also rejects Claims 4 and 10 as being unpatentable over Sutton in view of Gustafson et al. (US Patent No. 5,413,939, hereinafter Gustafson). In particular, the Examiner asserts that Sutton teaches latex particles which facilitate attachment of proteins or other biological compounds, but does not disclose that the solid phase is a surface on a biodisc or attached to a biodisc. The Examiner alleges that Gustafson teaches latex particles coupled to a binding pair, wherein one member of the pair is an analyte sought to be measured. According to the Examiner, Gustafson discloses measuring the presence of the analyte by detecting specific

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binding between the analyte and an anti-analyte (the second member of the binding pair), including protein and DNA, which is covalently bound to a surface of a solid phase that is usually a disc. The Examiner contends that one of ordinary skill in the art would have a reasonable expectation of success in using the latex particles on a solid phase support disk in the method of Sutton, since both Sutton and Gustafson teach latex particles covalently bound with proteins.

Finally, the Examiner rejects Claim 9 as being unpatentable over Sutton in view of Heinonen et al. (US Patent No. 5,912,342, hereinafter Heinonen). Specifically, the Examiner asserts that Sutton teaches copolymers, including polystyrene polymers, that facilitate attachment of biological compounds, but does not disclose a copolymer with a linker comprising at least one polyethylene glycol moiety. According to the Examiner, Heinonen teaches that polyethylene glycol can be grafted onto polystyrene in order to react with and form covalent linkages with chemical compounds. The Examiner alleges that it would have been obvious to one of ordinary skill in the art to modify the method of Sutton with polyethylene glycol that can be grafted onto polystyrene in order to covalently bind chemical compounds. Further, the Examiner contends that one of skill in the art would have a reasonable expectation of success in using polyethylene glycol since Sutton teaches polystyrene polymers that covalently bind proteins, and since Heinonen teaches that polyethylene glycol can be grafted onto polystyrene for covalent binding of molecules.

Applicants respectfully submit that Claims 3, 4, 9 and 10 are not obvious. To establish a *prima facie* case of obviousness the Examiner must show the following: (1) the prior art reference must teach, or must suggest all the claim limitations; (2) there must be some suggestion or motivation, either in the references or in the knowledge generally available among those of ordinary skill in the art, to modify the reference; and (3) there must be a reasonable expectation of success found in the prior art. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991).

Applicants have cancelled Claims 3, 4 and 10, thereby obviating the rejection of these claims. However, Applicants note that Claim 1 has been amended to incorporate a biodisc element similar to the biodisc element in original Claims 4 and 10. Applicants submit that amended Claim 1 is not obvious over Sutton in view of Gustafson. In particular, there is no suggestion or motivation to modify the method of Sutton based on Gustafson. Gustafson discloses that the anti-analyte can be bound in a variety of ways to the surface of a solid support,

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such as a disc, for use with an interferometer (see column 20, lines 12-18). Although Gustafson states that anti-analytes can be attached to the surface by essentially any bonding interaction, it is clear from the reference that the type of bonding forces used to attach the anti-analyte to the solid surface is unimportant to the author. The remainder of this reference describes assays for detecting analyte which rely on fact that portions of the disc are coated with anti-analyte and other areas are not. A skilled artisan, having read both Gustafson and Sutton, would not be motivated to apply the methods disclosed in Sutton to the interferometer discs described in Gustafson because discs that include predominately non-covalently bound anti-analyte are considered suitable for the applications described in Gustafson. As such, there exists no motivation to combine the disclosure of Gustafson with that of Sutton.

Applicants submit that Claim 9 is not obvious over Sutton in view of Heinonen. Specifically, the combination of Sutton and Heinonen fails to teach all the limitations of Claim 9. As stated above, Sutton does not teach or suggest measuring the amount of probe that binds to a solid phase in the absence of a cross-linking agent. Likewise, Heinonen does not disclose this step. As such, the combination of Sutton and Heinonen does not render Claim 9 obvious.

In view of the foregoing remarks, Applicants respectfully request that the Examiner reconsider and withdraw all rejections under 35 U.S.C. § 103(a).

### **Double Patenting**

The Examiner has provisionally rejected claims 1-10 as being unpatentable over Claims 1-15 of co-pending Application No. 10/086,941.

In response to a restriction requirement issued in co-pending Application No. 10/086,941, Applicants elected to prosecute Claims 29-66 and 109-115 without traverse. Because the claims upon which the Examiner based the provisional double patenting are no longer presented for examination in Application No. 10/086,941, Applicants respectfully request that the provisional rejection be withdrawn.

### **CONCLUSION**

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, amendments to the claims, the reasons therefore, and arguments in support of the patentability of the pending claim set are presented above. Any

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claim amendments which are not specifically discussed in the above remarks are made in order to improve the clarity of claim language, to correct grammatical mistakes or ambiguities, and to otherwise improve the capacity of the claims to particularly and distinctly point out the invention to those of skill in the art. In light of the above amendments and remarks, reconsideration and withdrawal of the outstanding rejections is specifically requested. If the Examiner finds any remaining impediment to the prompt allowance of these claims that could be clarified with a telephone conference, the Examiner is respectfully requested to initiate the same with the undersigned.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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